Reviewer’s report

Title: Interstitial fluid pressure, vascularity and metastasis in ectopic, orthotopic and spontaneous tumours.

Version: 3 Date: 2 October 2007

Reviewer: Professor Rubin

Reviewer’s report:

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The term 'array' in the sentence 'in an array of murine and xenograft models,' seems to be an overstatement since a total of 4 tumor types were investigated.

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The following sentence is unnecessary since no data are provided or referenced: "to date almost 300 patients with cervix cancer have undergone measurement of tumour IFP and other microenvironmental parameters prior to treatment."

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"Fluid that leaks from the vessels accumulates in the interstitium and causes the pressure to rise. However, there is probably wide variability in each of these parameters among individual tumours, which contributes to heterogeneity in IFP values."

This sentence and the following section are unclear. The conclusion that IFP merely reflect capillary pressure and vascular blood flow resistance ("Variation in IFP among tumours then mainly reflects differences in the underlying capillary pressure and vascular blood flow resistance.") seems to be an overstatement that is not supported by data. Direct measurements of IFP versus capillary hydrostatic pressure inside by micropuncture are lacking, thus little is known of capillary pressures inside tumors. It is also unclear to what extent tumor vessels are more leaky for fluid and salts than normal vessels. Normal vessels are permeable for fluid and salts but restrain protein capillary-to-interstitium transport. Tumor vessels may have a 'normal' permeability for fluid and salts but are pathologically leaky for proteins. In many tumors this seems to be due to a deregulated and high availability of VEGF. The suggestion that leaky vessels (leaky for fluid) would result in a high IFP is not in line with the Starling hypothesis. I suggest that this segment is rephrased or omitted.

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)